Remarks

Claims 1-9 and 32-47 remain pending. Claims 10-31 have been cancelled. In the Office Action of June 10, 2004, the Examiner acknowledged that claims 35, 36, 42, and 44 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. In Amendment C, filed August 10, 2004, applicant attempted to comply with these instructions, but in an Advisory Action of Sept. 13, 2004, the Office refused to enter these amendments after final. Claims 35, 36, 42, or 44 have not been the subject of a rejection by the Office.

Claims 48-49 have been added. Claims 2-6, 8-9, and 32-47 have been amended to include multiple dependencies to new claims 48 and/or 49.

Independent claim 48 has been drafted to recite all requirements of claim 35 and all intervening claims, in accord with the Office's prior acknowledgement that claim 35 would be allowable if rewritten in independent form.

Independent claim 49 has been drafted to recite all requirements of claim 42, and alternatively claim 44, and all intervening claims, in accord with the Office's prior acknowledgement that claims 42 and 44 would be allowable if rewritten in independent form.

REJECTION OF CLAIMS 1-9 UNDER 35 U.S.C. §103(A)

Reconsideration is requested of the rejection of claims 1-9 under 35 U.S.C. 103(a) over Massey et al. (WO 99/51780). To support an obviousness rejection, the Office must explain why the prior art would "appear to show the *claimed subject matter*," and not simply the general aspects of the invention.[1]

Massey et al. disclose a method for inhibiting the growth of a target cell contained within a mammal. While Massey et al. generally refer to a target cell as one harmful to an animal or human in which it occurs, they do not identify a fungal cell as a target cell nor do they describe target cells in a manner which would suggest that a

[1] *In re Rhinehart*, 531 F.2d 1048, 189 USPQ 143, 147 (C.C.P.A. 1976).

fungal cell falls within the class of cells they characterize as target cells. In describing target cells, Massey et al. state:

> "A target cell can be a tumor cell or other neoplastic cell, a parasite-infected cell or a pathogen-infected cell or a newly fertilized egg. The pathogen or parasite can be viral, bacterial, fungal or protozoan."[2]

In addition, the "the target cell ... is characterized in that it exhibits at least one component on its cell surface which differs from a normal comparison cell."[3] Massey et al. explain that "tumor cells and most infected cells generally express different markers or proteins on their surface than do normal or uninfected of the same type."[4] In their working examples, the target cells were animal tumor cells, specifically EMT-6 tumor cells, B16 melanoma cells, or MCA-205 sarcoma cells growing in mice.[5] One prophetic example suggests using animal cells (e.g., mouse) infected with an HIV viral pathogen.[6] Significantly, there are no working or prophetic examples in which the target cell is anything but an animal cell. Similarly, in their figures, Massey et al. report data relevant only to animal, specifically mouse, tumor target cells. It is clear from these characterizations that Massey et al.'s target cells are either (i) a human or animal tumor cell or (ii) a human or animal cell infected with a pathogen or parasite. In summary, nowhere do Massey et al. disclose or suggest that a target cell can be a fungal cell.

Massey et al.'s method involves four steps. First, the target cell, for example a human or animal cell infected with a parasite or pathogen (e.g., a fungus), is contacted with a peptide expression library covalently linked to a carrier. Second, peptides that bind to the surface of the human or animal target cell are recovered. Third, the recovered peptides are administered to a human or animal having target cells to be inhibited in growth. And fourth, the human or animal is allowed to develop an immunological response to the administered peptide. This method, according to

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[2] Massey et al. WO 99/51780, p. 8, ln. 11-13.

[3] *Id.* at p. 4, ln. 1-3. Similarly, Massey et al. state that it is "required by the present invention that the target cell have at least one component on its surface which distinguishes it from a comparable normal cell or tissue. *Id.* at p. 8, ln. 14-16; *see* p. 9, ln. 16-21)

[4] *Id.* at p. 9., ln 16-18.

[5] *Id.* at p. 10, ln. 12-16; p. 13, ln. 3-5; Example 3; Example 4.

[6] *Id.* at Example 5.

Massey et al., inhibits the growth of the target cell due to the immunological response of the animal or human.

In contrast, claim 1 is directed to a "method for identification of non-immunoglobulin peptides having an affinity for the surface of a fungus." Claim 1 requires: (a) constructing a library of peptides on the surface of a vector (*e.g.*, a phage display library); (b) contacting the vector with a **target fungus** and removing unbound vector; (c) eluting the bound vector **from the fungus**; (d) amplifying the bound vector; (e) sequencing the oligonucleotides in the eluted vector; (f) deducing the amino acid sequence of these oligonucleotides; and (g) selecting the non-immunoglobulin peptides from among the sequenced oligonucleotides. Massey et al. fail to disclose or suggest several of these requirements.

Massey et al. do not disclose or suggest contacting the library of peptides on the surface of a vector with a target fungus. Instead, Massey et al. merely disclose contacting a library of peptides on a carrier (*i.e.*, vector) with the surface of a human or animal cell that is infected with a pathogen, but not the pathogen itself.

As noted by the Office, Massey et al.'s claim 4 specifically recites a fungus but the Office is mistaken in its interpretation that a fungal cell is a target cell. Claim 4 of Massey et al. is reproduced here for the convenience of the Office:

> 4. The method of claim 1 wherein the target cell is a cell infected with a virus, a bacterium, a fungus or a protozoan.

In the specification, Massey et al. define a target cell as follows:

> "A target cell can be a tumor cell or other neoplastic cell, a parasite-infected cell or a pathogen-infected cell or a newly fertilized egg. The pathogen or parasite can be viral, bacterial, fungal or protozoan."[7]

Thus, the proper interpretation of claim 4 is that the target cell is a cell infected with (i) a virus, (ii) a bacterium, (iii) a fungus, (iv) or a protozoan. Given this interpretation, it is clear that Massey et al. only disclose contacting the peptide library with the surface of a

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[7] *Id.*

human or animal cell infected with a parasite or pathogen (e.g., a fungus), but not the parasite or pathogen itself.

Massey et al. do not disclose or suggest eluting the bound vector from the fungus. Massey et al. do not target a fungal cell, but rather a human or animal cell that has been infected with a parasite or pathogen (*e.g.*, a fungus). At most, Massey et al. disclose eluting bound carrier (*i.e.*, vector) from the human or animal cell target to which it bound. And because Massey et al. never targeted nor suggested targeting a fungal cell, they could not have suggested **eluting bound vector from a fungal cell**.

Massey et al. do not disclose or suggest selecting non-immunoglobulin peptides from among the sequenced oligonucleotides. Massey et al. fail to discriminate among binding peptides on the basis of whether they are immunoglobulin or non-immunoglobulin polypeptides. Furthermore, Massey et al. do not even identify peptides (immunoglobulin or non-immunoglobulin) that bind to the surface of fungi.

Massey et al. do not disclose deducing the amino acid sequence of peptides encoded by the oligonucleotides contained in the eluted vector. Massey et al. allude to the use of "peptides derived in sequence" from carrier proteins in the preparation immunogenic compositions.[8] But, Massey et al. do not describe sequencing oligonucleotides eluted from the surface of a fungus, as required by claim 1.

In the June 10, 2004 Final Rejection, the Office erroneously asserts that Applicant argued "that the anti-fungal peptides identified by the method of claim 1 inhibits fungal growth/proliferation by a direct interaction." Applicant never made such an argument in the Amendment B and Response of March 15, 2004. It appears that the Office wrongfully focused upon the "mechanism of growth inhibition of fungus," devoting the majority of its response to rebutting an argument Applicant did not make, while at the same time failing to address Applicant's actual argument. Put simply, Applicant's argument is that Massey et al. do not disclose or suggest targeting the surface of a fungal cell. Rather, Massey et al. merely target the surface of a human or animal cell infected by a pathogen.

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[8] *Id.* at p. 15, ln. 5-6; *see* p. 17, ln. 17-18.

Massey et al. also fail to disclose or suggest the requirements of claims which depend from claim 1. For example, claim 5 requires that the **sequence of oligonucleotides inserted into the vector be of the sequence GCA GNN (NNN)7 or the sequence of SEQ ID NO:1** and claim 8 requires **determination of the binding affinity of the identified peptides to the target fungus**. Massey et al. do not disclose or suggest either of these features. Furthermore, Massey et al. could not determine the binding affinity to a fungus because they never target a fungal cell.

In summary, Massey et al. do not disclose or suggest several requirements of claim 1, including contacting the library of peptides on the surface of a vector with a target fungus; eluting the bound vector from the fungus; and selecting the non-immunoglobulin peptides from among the sequenced oligonucleotides that bound the target fungus. Thus, claim 1 and the claims which depend therefrom are patentably distinct from Massey et al., and this reference cannot, as a single reference, support an obviousness rejection.

REJECTION OF CLAIMS 32-34, 37-41, 43, 45-47 UNDER 35 U.S.C. §103(A)

Reconsideration is requested of the rejection of claims 32-34, 37-41, 43, and 45-47 under 35 U.S.C. § 103(a) over Massey et al. (WO 99/51780) in view of Gough et al. (J. Immuno. Met. (1999) 228, 97-108). In rejecting these claims, the Office asserts it would have been obvious to employ *Phytophthora*, as disclosed by Gough et al., in the method of Massey et al.[9]

An obviousness rejection based upon a combination of references cannot require substantial reconstruction or redesign of the references to arrive at the claimed invention.[10] Plant pathogenic fungi, for example *Phytophthora* as disclosed in Gough et al., cannot be combined with the method of Massey et al. This is because the method of Massey et al. is directed to human or animal cells infected by a pathogen. Applicant is not aware of any literature report or other source to suggest or show that *Phytophthora* can infect a human or animal cell. The Office has failed to demonstrate

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[9] Final Office Action, p. 4.
[10] *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

how *Phytophthora*, a plant pathogen presumptively unable to infect a human or animal cell, could be used in the methods of Massey et al. Absent such a showing, these references cannot properly be combined to support an obviousness rejection.

Where references can theoretically be combined, the resulting combination or modification must appear to show or suggest the claimed invention.[11] Even if *Phytophthora*, or another fungi or plant pathogenic fungi, were able to infect a human or animal cell, the use of Gough et al.'s pathogens in Massey et al.'s process would not result in the method defined by claims 32-34, 37-41, 43, and 45-47. Claim 1, from which these claims depend, requires contacting the peptide library with the surface of the target fungus; in contrast, if Massey et al. and Gough et al. were combined as suggested by the Office, this would merely lead to contacting a library of peptides with a **human or animal cell** infected with Gough et al.'s fungus. And, for the reasons noted above in the context of the rejection of claim 1, using Gough et al.'s fungus as a pathogen in Massey et al.'s process would not lead to the elution of bound vector from a fungus (as required by claim 1) because, according to these methods, the peptides would never be exposed to the fungus. The combination similarly fails to suggest selecting non-immunoglobulin peptides (from among the sequenced oligonucleotides that bound the target fungus, as required by claim 1 and all claims dependent upon claim 1); in fact, neither Massey et al. nor Gough et al. even mentions discriminating between immunoglobulin peptides and non-immunoglobulin peptides for any reason.

Claim 32 further requires the **target fungus to be a plant pathogenic fungus**. As discussed above, Massey et al. target human or animal cells infected with a parasite or pathogen (fungi merely being identified as one such parasite or pathogen) and not the pathogen directly. Furthermore, plant pathogenic fungi are presumably unable to infect human or animal cells and the Office has not demonstrated otherwise. This argument applies equally to claims 33-34, which require the target fungus to be *Phytophothora* or several species of *Phytophothora*.

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[11] *In re Wright*, 848 F.2d 1216, 6 USPQ2d 1959, 1962 (Fed. Cir. 1988); *In re Nielson*, 816 F.2d 1567, 2 USPQ2d 1525, 1528 (Fed. Cir. 1987).

Claim 37 requires **contacting the target fungus at different life stages**. Massey et al. not only fail to contact a fungus at various life stages, they fail to suggest contacting at any life stage. Furthermore, Massey et al.'s process relies upon the a parasite or pathogen infecting target cells, and fungi generally are not infectious during all life stages. These arguments apply also to claims 38-40, each requiring different life stages of the fungus, including oospore, chlamydospore, zoospore, and germling life stages.

In conclusion, the Office has not demonstrated that Gough et al.'s fungus may even be used as a parasite or pathogen in Massey et al.'s process. But even if it were possible for Gough et al.'s fungi to infect a human or animal cell, the combination of these references as put forth by the Office does not lead to the invention defined by claim 1, the requirements of which are incorporated into claims 32-34, 37-41, 43, and 45-47. Further, when considered in combination Massey et al. and Gough et al. do not disclose or suggest the additional requirements of, for example, claims 32-34 and 37-40. Accordingly, this combination of references does not support the obviousness rejection asserted by the Office.

CONCLUSION

In light of the foregoing, Applicants request an entry of the claim amendments and solicit allowance of the claims. The Office is invited to contact the undersigned attorney should any issue remain unsolved.

The Commissioner is hereby authorized to charge any fee deficiency in connection with this Response to Deposit Account Number 19-1345.

Respectfully submitted,

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